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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/441,443	05/15/95	HOUGHTON M	0063.024

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EXAMINER	
ZEMAN, M	
ART UNIT	**PAPER NUMBER**
1631	21

DATE MAILED: 04/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/441,443	Applicant(s) HOUGHTON ET AL.	
	Examiner Mary K Zeman	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *01 December 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-48 and 52-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-48 and 52-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☐ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). ____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other:

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit **1631**.

Claims 40-48 and 52-59 are pending in this application. Claims 49-51 have been canceled.

In view of the filing of a proper terminal disclaimer, the rejection of the claims under obviousness type double patenting over 5,714,569 is withdrawn.

New Grounds of Rejection

Claims 40-48 and 52, 56-59 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial asserted utility or a well established utility.

The claims are drawn to compositions of antisense polynucleotides, and a method of inhibiting viral replication using those polynucleotides. These antisense polynucleotide compositions lack a specific and substantial utility as required.

The test for utility is a three pronged test wherein the categories tested are: a specific utility, a substantial utility and a credible utility. The specific asserted utility for the claimed compositions is as antisense molecules. This utility does not meet the standards for specific or substantial utility. Applicant is directed to the Revised Interim Utility Guidelines, Federal

Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999. In keeping with the revised utility guidelines and corresponding training materials (available on the PTO Website), none of the claimed uses is a specific and/or substantial use.

While applicant asserts specific utilities for the claimed invention (antisense, and methods of inhibiting viral replication), these are not considered to be substantial utilities for the following reasons. These utilities are premised on the assumption that the simple disclosure of the HCV sequence provides ample utility for antisense polynucleotides of that sequence.

Antisense technology is quite unpredictable, especially in the area of antiviral activity, as evidenced by the art previously cited: Branch 1998 TIBS Vol 23 pp 45-50. Branch discusses the inoperability of most antisense oligonucleotides in vitro and in vivo (Claim 52 is broad enough to encompass in vivo/ gene therapy applications), and the inability to predict what sequences would be useful as antisense molecules. While Applicant has defined various oligonucleotide sequences, the specification fails to support their asserted utility as antisense molecules. The specification does not set forth any teaching of an antisense molecule preventing replication in any system, nor does the art recognize that those oligonucleotides would credibly be used as antisense molecules. One of skill in the art of antisense technology would not accept the recited use as being currently available, or able to be used successfully for the inhibition of replication of HCV, nor is the technology so well established that one of skill in the art would be fully versed in how to use the invention, as claimed. As such, further research would be required to identify or reasonably confirm a "real world" context of use. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved

would be required. Therefore, the specification does not fairly disclose a substantial utility for the claimed embodiments.

Applicant argues that the recitation at page 78 of the specification is sufficient teaching of what portions of the genome antisense molecules should target, however there is no indication of what regions of DNA would be useful in targeting such activities as the broad recitation of "block protein translation" and "prevent viral replication". No portions of the HCV genome which would be useful to prevent or block these viral replications steps are indicated or even hinted at in the specification. The information recited in section II.H does not further illuminate how to chose antisense polynucleotides which would block or prevent protein translation or viral replication. Section II.H deals with the selection of probes and primers, which would not necessarily perform any antisense functions.

Each of the sections pointed out by Applicant are vague prophetic recitations which indicate that antisense polynucleotides could be found or identified, however, no such antisense polynucleotides are taught in the specification.

Applicant has not provided guidance as to what portions of the genome would be useful as antisense polynucleotides. The prior art does not provide any antisense polynucleotides of HCV, and the skilled artisan could not predict those sequences. The unpredictability of the antisense art is further illustrated by Branch, A.D. A good antisense molecule is hard to find. 1998 TIBS vol 23 pp 45-50) Branch reviews the many problems inherent in selecting antisense molecules which will target the intended processes in vitro and in vivo. Branch even speaks specifically to problems with antisense technology as it relates to HCV at page 48:

> "One anecdote reveals how the redundancy of biological sequences could plague antisense methods. A conserved region at the 5' end of the hepatitis C virus is considered to be a potential target for antisense drugs. This short region contains a particular 10-mer that is also present in 62 known human mRNAs (citation omitted), and it contains two 17-mers that occur in known human DNA sequences."

The specification, as filed, does not point out oligonucleotides of 8, 10, 12, 15 or 20 nucleotides that would be suitable for use as antisense polynucleotides. There is no direction as to which sequences should be selected from the approximately 9Kb of HCV sequence. There is no teaching as to which portions of the HCV genome would be susceptible to an antisense blockage and therefore a suitable region from which the polynucleotide could be selected, nor is there an indication as to what length of oligonucleotide is preferred. There is no recitation of particular sequences of polynucleotides useful in the practice of the invention. It is apparent that the polynucleotides may comprise other, non-HCV sequences, as long as there is a stretch of HCV sequence within, which further broadens the scope of the claims. The very large number of potential polynucleotides covered by the scope of the pending claims is an invitation to experiment with the 9000+ nucleotides of HCV-1 and any other HCV or non-HCV sequence, to find polynucleotides which are capable of acting as antisense polynucleotides in the practice of the invention. Therefore, the specification fails to describe and support the breadth of the pending claims.

Claims 40-48 and 52, 56-59 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 53-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 53-55 are drawn to compositions comprising an antisense polynucleotide and an antiviral agent.

The specification, as filed, does not set forth compositions of antisense molecules in combination with antiviral agents, such that one of ordinary skill in the art would readily be able to use the claimed invention.

As set forth above, antisense technology is quite unpredictable, especially in the area of antiviral activity, as evidenced by the art previously cited: Branch 1998 TIBS Vol 23 pp 45-50. Branch discusses the inoperability of most antisense oligonucleotides in vitro and in vivo (Claim 52 is broad enough to encompass in vivo/ gene therapy applications), and the inability to predict what sequences would be useful as antisense molecules.

Applicant has previously pointed to Section II.H in the specification for support for the claimed invention. The information recited in section II.H does not further illuminate how to

chose antisense polynucleotides which would block or prevent protein translation or viral replication. Section II.H deals with the selection of probes and primers, which would not necessarily perform any antisense functions. The further selection of an antiviral agent to combine with the antiviral is not disclosed, nor are any antiviral agents tested or identified which have any effect on HCV replication.

Each of the sections pointed out by Applicant are vague prophetic recitations which indicate that antisense polynucleotides could be found or identified, however, no such antisense polynucleotides are taught in the specification.

Applicant has not provided guidance as to what portions of the genome would be useful as antisense polynucleotides, nor what agents would be useful, and how to use this composition. The prior art does not provide any antisense polynucleotides of HCV, and the skilled artisan could not predict those sequences. The unpredictability of the antisense art is further illustrated by Branch, A.D. A good antisense molecule is hard to find. 1998 TIBS vol 23 pp 45-50) Branch reviews the many problems inherent in selecting antisense molecules which will target the intended processes in vitro and in vivo. Branch even speaks specifically to problems with antisense technology as it relates to HCV at page 48:

The specification, as filed, does not point out oligonucleotides of 8, 10, 12, 15 or 20 nucleotides that would be suitable for use as antisense polynucleotides. There is no direction as to which sequences should be selected from the approximately 9Kb of HCV sequence. There is no teaching as to which portions of the HCV genome would be susceptible to an antisense blockage, or antiviral agent activity and therefore a suitable region from which the

polynucleotide could be selected, nor is there an indication as to what length of oligonucleotide is preferred. There is no recitation of particular sequences of polynucleotides useful in the practice of the invention. It is apparent that the polynucleotides may comprise other, non-HCV sequences, as long as there is a stretch of HCV sequence within, which further broadens the scope of the claims. The very large number of potential polynucleotides covered by the scope of the pending claims is an invitation to experiment with the 9000+ nucleotides of HCV-1 and any other HCV or non-HCV sequence, to find polynucleotides which are capable of acting as antisense polynucleotides in the practice of the invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308 4028.

The fax number for this Art Unit is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

mkz
April 21, 2000

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
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